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(54) Title: PHARMACEUTICAL FORMULATION OF OLANZAPINE

(57) Abstract: A pharmaceutical formulation comprising a homogeneous mixture of (a) olanzapine or a pharmaceutically acceptable salt thereof as an active ingredient, (b) a monosaccharide and/or oligosaccharide, (c) a polysaccharide and, optionally, further ingredients .

# INTERNATIONAL SEARCH REPORT

Intern. Application No  
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**A. CLASSIFICATION OF SUBJECT MATTER**  
**IPC 7 A61K9/20 A61K31/551 A61P25/18**

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**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
**IPC 7 A61K A61P**

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, MEDLINE, EMBASE

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 830 858 A (LILLY CO ELI) 25 March 1998 (1998-03-25) cited in the application page 5, line 1-51; example 3 -----	1-11, 14-16
E	WO 03/086361 A (DESHMUKH ABHIJIT MUKUND ; DHANORKAR VIPIN TATYASAHEB (IN); DIVI MURALI) 23 October 2003 (2003-10-23) example 7-9 example 13 -----	1,8,10, 11,15,16

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

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Information on patent family members

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Patent document cited in search report	Publication date	Patent family member(s)		Publication date
EP 0830858	A 25-03-1998	AU	719788 B2	18-05-2000
		AU	4423097 A	17-04-1998
		BR	9713215 A	04-04-2000
		CA	2266448 A1	02-04-1998
		CN	1230883 A	06-10-1999
		CZ	9900988 A3	15-12-1999
		EA	1610 B1	25-06-2001
		EP	0830858 A1	25-03-1998
		HU	9904065 A2	28-04-2000
		ID	21762 A	22-07-1999
		JP	2001501207 T	30-01-2001
		KR	2000048540 A	25-07-2000
		NO	991405 A	23-03-1999
		PL	332503 A1	13-09-1999
		TR	9900651 T2	21-07-1999
		WO	9813027 A1	02-04-1998
		US	2001020032 A1	06-09-2001
		ZA	9708517 A	23-03-1999
WO 03086361	A 23-10-2003	WO	03086361 A1	23-10-2003

**Claims**

1. A pharmaceutical formulation comprising a homogeneous mixture of (a) olanzapine or a pharmaceutically acceptable salt thereof as an active ingredient, (b) a monosaccharide and/or oligosaccharide, and (c) a polysaccharide.
2. The pharmaceutical formulation of claim 1 comprising 40 to 80 weight % of the component (b).
3. The pharmaceutical formulation of any one of claims 1 to 2 comprising 10 to 40 weight % of the polysaccharide.
4. The pharmaceutical formulation of any one of claims 1 to 3 additionally comprising (d) up to 15 weight % of a disintegrant.
5. The pharmaceutical formulation of any one of claims 1 to 4 additionally comprising (e) 5 to 20 weight % of a binder.
6. The pharmaceutical formulation of any one of claims 1 to 5 additionally comprising (f) 0.25 to 5 weight % of a lubricant.
7. The pharmaceutical formulation of any one of claims 1 to 6 additionally comprising (g) 0.1 to 0.5 weight % of a glidant.
8. The pharmaceutical formulation of any one of claims 1 to 7, wherein the component (b) is selected from the group consisting of lactose, sucrose, dextrose, sorbitol, mannitol, lactitol, and mixtures thereof.
9. The pharmaceutical formulation of claim 8, wherein the component (b) is lactose.

10. The pharmaceutical formulation of any one of claims 1 to 9, wherein the polysaccharide is selected from the group consisting of starch, cellulose, and mixtures thereof.
11. The pharmaceutical formulation of claim 10, wherein the polysaccharide is cellulose.
12. The pharmaceutical formulation of claim 11, wherein a mixture of 20 to 30 weight % of cellulose and 70 to 80 weight % of lactose is used as the components (b) and (c).
13. The pharmaceutical formulation of claim 12 comprising  
70 to 90 weight % of a mixture of 20 to 30 weight % of cellulose and 70 to 80 weight % of lactose;  
8 to 12 weight % of a binder;  
3 to 10 weight % of a disintegrant;  
0.3 to 2 weight % of a lubricant; and  
0.2 to 0.4 weight % of a glidant.
14. The pharmaceutical formulation of any one of claims 1 to 13 obtainable by direct compression.
15. The pharmaceutical formulation of any one of claims 1 to 14 comprising olanzapine as the only pharmaceutically active ingredient.
16. The pharmaceutical formulation of any one of claims 1 to 15 having the form of an uncoated tablet.
17. A process for preparing a stable pharmaceutically solid oral formulation according to any one of claims 1 to 16 comprising combining (a) olanzapine or a pharmaceutically acceptable salt thereof with (b) a monosaccharide and/or oligosaccharide, (c) a polysaccharide and optionally one or more of components (d) to (g), followed by a direct compression of the mixture into tablets in the absence of any solvent.